In view of the preceding amendments and the remarks which follow, applicants respectfully request that the Examiner reconsider and withdraw the rejections set forth in the April 24, 2001 Office Action, and earnestly solicit allowance of the claims currently under examination, namely, Claims 1-11.

Oath/Declaration

In the Office Action, the Examiner indicated that the oath or declaration was defective. Applicants note that two (2) Supplemental Declarations were filed with the U.S. Patent Office on November 29, 2000, in connection with the above-identified application, in order to correct the defect in the original Declaration. Attached hereto, as Exhibit A, is a copy of all correspondence to the U.S. Patent Office concerning the two Supplemental Declarations that were filed on November 29, 2000. Applicants believe that the Supplemental Declarations should be sufficient to overcome the defect in the original Declaration, and that a new Declaration is not necessary.

35 U.S.C. §112, 2nd Paragraph Rejection

Claims 1-11 were rejected under 35 U.S.C. §112, second paragraph. Applicants have amended Claims 1, 3, and 7 in accordance with the Examiner's suggestions. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

35 U.S.C. §102(b) Rejection

Claims 1, 2, 10, and 11 were rejected under 35 U.S.C. §102(b), as being anticipated by Cancroft *et al.* (1973), as evidenced by Socolow *et al.* (1967), Tazebay *et al.* (2000), and Spitzweg *et al.* (1998). Applicants respectfully traverse this rejection.

The claimed invention is directed to a method for diagnosing breast cancer in a non-lactating subject, comprising determining whether or not mammary gland sodium/iodide symporter (mgNIS) is expressed in breast tissue of the subject. The detection of expression of mgNIS in the breast tissue is indicative of breast cancer in the subject, while no detection of expression of mgNIS in the breast tissue is indicative of the absence of breast cancer in the subject. The claimed invention was not taught by Cancroft *et al.*

Cancroft *et al.* described the use of scintigraphic imaging and ^{99m}Tc-pertechnetate to differentiate between benign and malignant breast masses. Specifically, Cancroft *et al.* showed that malignant breast masses have a greater ^{99m}Tc-pertechnetate uptake than do benign breast masses, which have a lesser uptake of ^{99m}Tc-pertechnetate. However, significantly, Cancroft *et al.* did not utilize any normal, healthy subjects as controls, and did not assess whether or not breast tissue from normal, healthy subjects does or does not take up ^{99m}Tc-pertechnetate. Therefore, Cancroft *et al.* did not establish a method for diagnosing breast cancer; at most, Cancroft *et al.* taught a method for differentiating benign and malignant breast masses. For these reasons alone, the claimed invention is not anticipated by Cancroft *et al.*

In addition, the method of the claimed invention requires that detection of expression of mgNIS in breast tissue of a subject is indicative of breast cancer in the subject, while no detection of expression of mgNIS in the breast tissue is indicative of the absence of breast cancer in the subject. Cancroft *et al.* did not teach or suggest that mgNIS expression is detectable in breast cancer tissue, but not in normal, non-lactating

breast tissue. Accordingly, for this reason as well, the claimed invention is not anticipated by Cancroft *et al.*

Finally, the Examiner cited Socolow *et al.*, Tazebay *et al.*, and Spitzweg *et al.* in support of his position that expression of mgNIS is inherent in ^{99m}Tc-pertechnetate uptake, as disclosed in the Cancroft *et al.* publication. In order for a reference to constitute an inherent anticipation under United States patent law, the inherent characteristics must necessarily flow from the reference's teachings. *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991). The Examiner has not demonstrated that the increased uptake of ^{99m}Tc-pertechnetate in the malignant breast masses described in Cancroft *et al.* necessarily resulted from mgNIS expression.

For the foregoing reasons, Cancroft *et al.* does not anticipate the claimed invention. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

35 U.S.C. §103(a) Rejection

The Examiner also rejected Claims 1-11 under 35 U.S.C. §103(a), as being unpatentable over Cancroft *et al.* (1973), in view of Eskin *et al.* (1974), Spitzweg *et al.* (1998), and Jhiang *et al.* (1998). Applicants respectfully traverse this rejection, and submit that none of the references cited by the Examiner, either alone or in combination, teaches or suggests the claimed method.

Cancroft *et al.* described the use of scintigraphic imaging and ^{99m}Tc-pertechnetate to differentiate between benign and malignant breast masses. Cancroft *et*

al. did not teach or suggest that mgNIS expression is detectable in breast cancer tissue, but not in normal, non-lactating breast tissue. Eskin *et al.* disclosed that breast cancer tissue takes up more radiolabelled iodide than does normal breast tissue in the same patient. However, like Cancroft *et al.*, Eskin *et al.* did not teach or suggest that mgNIS expression is detectable in breast cancer tissue, but not in normal, non-lactating breast tissue.

Spitzweg *et al.* analyzed human NIS (hNIS) gene expression in various non-thyroid tissues, and found hNIS expression in the mammary gland taken from normal human tissues (*see* p. 1748). Although we can only speculate as to why Spitzweg *et al.* detected hNIS expression in normal mammary gland, it is important to understand that Spitzweg *et al.* did not demonstrate that mgNIS expression is detectable in breast cancer tissue, but not in normal, non-lactating breast tissue. Jhiang *et al.* described the distribution and cellular localization of hNIS in tissue from the thyroid and salivary glands. However, like Spitzweg *et al.*, Jhiang *et al.* did not demonstrate detectable mgNIS expression in breast cancer tissue, and the absence of detectable mgNIS expression in normal, non-lactating breast tissue.

In summary, neither Cancroft *et al.*, Eskin *et al.*, Spitzweg *et al.*, nor Jhiang *et al.*, either alone or in combination, established that mgNIS expression is detectable in breast cancer tissue, but not in normal, non-lactating breast tissue. For these reasons, the claimed invention is patentable over the references cited by the Examiner. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

No fee, other than the $460.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. If any additional fee is required to preserve the pendency of the subject application, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 01-1785.

Respectfully submitted,

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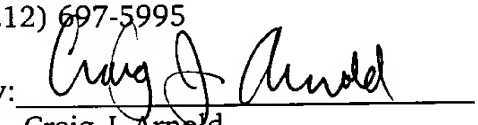
Dated: October 3, 2001
New York, New York

By: 
Craig J. Arnold
Reg. No. 34,287

SCHEDULE A

REDLINED VERSION

Please rewrite Claims 1, 3, and 7 as follows:

1. (amended) A method for diagnosing breast cancer in a non-lactating subject, comprising determining whether or not ~~detecting expression of~~ mammary gland sodium/iodide symporter (mgNIS) is expressed in breast tissue of the subject, wherein detection of expression of mgNIS in the breast tissue is indicative of breast cancer in the subject, and no detection of expression of mgNIS in the breast tissue is indicative of the absence of breast cancer in the subject.

3. (amended) The method of Claim 1, wherein the expression of mgNIS is detected using an agent ~~reactive with~~ that specifically and selectively binds to mgNIS.

7. (amended) The method of Claim 1, wherein the expression of mgNIS is detected using at least one nucleic acid probe ~~which hybridizes~~ that specifically and selectively hybridizes to nucleic acid encoding mgNIS.